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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/248,964	02/12/1999	KAI W. WUCHERPFENNIG	HUIP-P01-005	9407
28120	7590	09/22/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			VANDERVEGT, FRANCOIS P	
			ART UNIT	PAPER NUMBER

1644

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 09/248,964	Applicant(s) WUCHERPFENNIG ET AL.	
	Examiner F. Pierre VanderVegt	Art Unit 1644	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2004 and 14 May 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20, 103 and 114-147 is/are pending in the application.
- 4a) Of the above claim(s) 1-20 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 131-147 is/are allowed.
- 6) ☒ Claim(s) 103, 114-124 and 128-130 is/are rejected.
- 7) ☒ Claim(s) 125-127 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

This application claims the benefit of the filing date of provisional application 60/075,351 and is a continuation of PCT/US97/14503, which claims the benefit of the filing date of provisional application 60/024,007.

Claims 21-102 and 104-113 have been canceled previously.

New claims 134-147 have been added.

**Claims 1-20 stand as withdrawn.**

Claims 1-20, 103 and 114-133 are currently pending.

**Claims 103 and 114-147 are the subject of examination** in the present Office Action.

Applicant's arguments and the declaration of inventor Kai Wucherpfennig filed October 31, 2003 have been fully considered and only the following grounds of rejection are maintained.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

1. Claims 103, 114-123, 128 and 129 stand rejected under 35 U.S.C. 102(a) as being anticipated by Scott et al. (J. Exp. Medicine 183:2087-2095 (May 1996)), as evidenced by U.S. Patent No. 5,837,816 to Ciardelli et al.

It was previously stated: "Scott et al teach a murine IA Class II MHC fusion protein comprising a heterodimer, wherein the first polypeptide comprises a fusion of an extracellular domain of an MHC Class II alpha chain and a first coiled-coil dimerization domain; wherein the second polypeptide comprises a fusion of an extracellular domain of an MHC Class II beta chain and a second coiled-coil dimerization domain, as recited in claim 103, (see entire article, especially the Summary). Scott further teaches that human MHC Class HLA-DQ alleles, unlike HLA-DR alleles, are well known in the art to be promiscuous in their pairing behavior and are able to mismatch with HLA-DR chains (page 2087, column 1 in particular). Said fusion protein taught by Scott et al comprises a leucine zipper domain as recited by claim 122, (see entire article, especially the Summary). Scott also teaches said fusion protein further comprising an MHC binding peptide, wherein said peptide is bound to the MHC Class II fusion protein, as recited in claim 129 (see entire article, including page 2091). Claims 114-115 and 118-119 are included because, while Scott does not specifically disclose that the referenced MHC fusion protein comprises residues 5-180 or residues 5-200 of an MHC Class II alpha chain as recited in claims 114-115 or residues 5-185 or residues 5-205 of an MHC Class II beta chain as recited in claims 118-119, Scott teaches on page 2089, column 1, that the MHC Class II molecules were truncated at the transmembrane

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region. Accordingly, the segment of the MHC molecule utilized by Scott comprises the entire extracellular region and therefore inherently comprises the recited residues. Claim 128 is included because Scott teaches a flexible linker segment between the MHC domain and the dimerization domain that comprises alanine and serine as a majority of the amino acid residues (Figure 1A in particular). Claim 123 is included because the '816 patent teaches that a leucine zipper refers to a repetitive heptad motif containing 4-5 leucine residues (see entire patent including column 1, lines 55-60). The prior art anticipates the claimed invention. Claims 116, 117, 120 and 121 are included because, while Scott teaches that HLA-DR can form DR $\alpha$ /DR $\beta$  heterodimers without having to add a dimerization domain, in conditions where DQ  $\alpha$  and  $\beta$  chains are also present, according to Scott the DQ  $\alpha$  and  $\beta$  chains are promiscuous and will readily form a heterodimer with DR haplotypes. Accordingly, when DQ  $\alpha$  and  $\beta$  chains are present and the DR  $\alpha$  and  $\beta$  chains do not have dimerization domains to direct their preferential combination, DQ/DR heterodimers would be formed.

Applicant argues that the teachings of Scott are not applicable to human MHC studies because Scott teaches that methods that are successful for creating HLA-DR dimers are not effective for creating IA dimers due to the promiscuity of IA, substantially asserting that Scott teaches away from applying the method to human MHC. The Examiner respectfully disagrees with Applicant's position. Scott's teachings differentiate only between HLA-DR and IA, but not between IA and HLA-DQ. In fact, as addressed supra, Scott teaches that IA and HLA-DQ are similar in their properties, reasonably suggesting to the artisan that this method disclosed for IA would be applicable to practice on HLA-DQ as well. It is noted that the claims are drawn to all human MHC Class II, including HLA-DQ and not just HLA-DR."

Applicant's arguments filed October 31, 2003 have been fully considered but they are not persuasive.

Applicant argues that the Scott reference is not available as prior art because it was published less than one year prior to the filing of the provisional application to which the claimed invention claims priority and because Applicant conceived the instantly claimed invention prior to the publication of Scott. Applicant filed a declaration by inventor Kai Wucherpennig under 35 USC § 1.131 in evidence of this prior conception in an attempt to antedate the Scott reference.

However, Applicant's declaration under 35 USC § 1.131 is defective and therefore is not effective as evidence of prior conception. A declaration under 35 USC § 1.131 must be signed by ALL inventors of a claimed invention and the instant declaration was not signed by named co-inventor Jack Strominger. Furthermore, section 4 of the declaration casts the status of Jack Strominger as a co-inventor. Inventor Wucherpennig states that the work that is the subject matter of the claimed invention was performed under his direction. However, he does not identify which of the co-authors of the cited Kalandadze reference were under his direction. Accordingly, it appears that co-inventor Jack Strominger was also under his direction and it is therefore unclear why Jack Strominger is listed as a co-inventor, as the record now suggests that he did not contribute any inventive input.

This rejection and all other rejections based upon the Scott reference can be overcome by the filing of a proper declaration under 35 USC § 1.131.

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*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claim 103, 123 and 124 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Scott et al. in view of US Patent No. 5,837, 816 to Ciardelli et al.

It was previously stated: "Scott has been discussed supra. Scott does not teach that the leucine zipper domain is selected from the group consisting of a Fos and a Jun leucine zipper domain.

The '816 patent teaches that Fos and Jun comprise leucine zipper domains which preferentially form a heterodimer (see entire patent, especially column 4, lines 44-50).

Accordingly, it would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Scott regarding the manufacture of heterodimers of promiscuous MHC domains using linking domains with the teachings of the '816 patent regarding Fos and Jun leucine zipper domains. One would have been motivated with a reasonable expectation of success by the need to produce large quantities of human MHC Class II heterodimers for the study of immune recognition (Scott, Abstract in particular), the teaching of Scott that some human Class II haplotypes are promiscuous in the formation of heterodimers in a manner similar to murine IA haplotypes which can be joined by leucine zippers (page 2087 in particular) and the teaching of the '816 patent that Fos and Jun leucine zipper domains preferentially form a heterodimer which allows the formation of heterodimers of ectodomains with an affinity approaching the comparable cell surface complex (Abstract in particular)."

Applicant again asserts that the Scott reference is not available as prior art because it was published less than one year prior to the filing of the provisional application to which the claimed invention claims priority and because Applicant conceived the instantly claimed invention prior to the

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publication of Scott. However, the declaration under 35 USC § 1.131 is defective for the reasons stated supra.

3. Claims 103 and 130 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Scott et al. in view of US Patent No. 6,015,884 to Schneck et al.

It was previously stated: "Scott has been discussed supra. Scott does not teach that the MHC binding peptide is covalently bound to the MHC class II fusion protein.

The '884 patent teaches the covalent linkage of an MHC peptide to a soluble Class II heterodimer (see entire patent, especially Figure 1C) and that said heterodimer has potential use as an immune modulating agent (see entire patent, especially column 5, lines 29-32).

Accordingly, it would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Scott regarding the manufacture of heterodimers of promiscuous MHC domains using linking domains with the teachings of the '884 patent regarding the covalent linkage of an MHC peptide to a soluble Class II heterodimer. One would have been motivated, with a reasonable expectation of success, by the need to produce large quantities of human MHC Class II heterodimers for the study of immune recognition (Scott, Abstract in particular), the teaching of Scott that some human Class II haplotypes are promiscuous in the formation of heterodimers in a manner similar to murine IA haplotypes which can be joined by leucine zippers (page 2087 in particular) in order to study the interaction of the heterodimer with the MHC binding peptide in solution, for example by X-ray crystallography (Scott, page 2094 in particular)."

Applicant again asserts that the Scott reference is not available as prior art because it was published less than one year prior to the filing of the provisional application to which the claimed invention claims priority and because Applicant conceived the instantly claimed invention prior to the publication of Scott. However, the declaration under 35 USC § 1.131 is defective for the reasons stated supra.

### *Conclusion*

4. Claims 131-147 are allowed.


5. Claims 125-127 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.   
Patent Examiner  
September 20, 2004

  
PATRICK J. NOLAN, PH.D.  
PRIMARY EXAMINER

9/20/04